--CROSS REFERENCE TO RELATED APPLICATIONS

The present application is a continuation of U.S. Serial No. 09/938,700 filed August 24, 2001 which claims benefit of U.S. Provisional Application No. 60/228,989 filed August 30, 2000.--

## IN THE SPECIFICATION:

Please replace the paragraph on page 8, lines 26-27 as follows:

The antigenic peptides can be supplied by direct administration or indirectly as "[["]]pro-drugs[["]]" using somatic cell gene therapy.

Please replace the paragraph on page 13, lines 1-11 as follows:

The antigenic peptides of the present invention comprise an amino acid sequence of the CH3 domain of an IgE molecule or a fragment thereof and induce the production of anti-IgE antibodies, which are not anaphylactic. The present invention also encompasses antigenic peptides comprising an amino acid sequence of the junction of the CH3 and CH4 domains of an IgE molecule, which induce anti-IgE antibodies that are not anaphylactic. In particular, the antigenic peptides of the present invention induce the production of anti-IgE antibodies which bind to soluble (free) IgE in serum and other bodily fluids, prevent IgE from binding to its high affinity receptors on mast cells and basophils, and do not cross-link receptor-bound IgE. The antigenic peptides of the present invention may be coupled to one or more heterologous peptides. The antigenic peptides of the invention can be supplied by direct administration or indirectly as "[["]]pro-drugs[["]]" using somatic cell gene therapy.

Please replace the paragraph beginning on page 14, lines 19-33 as follows:

For example, one or more mutations at the nucleotide level which result in one or more amino acid mutations can be introduced by site-directed mutagenesis or PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "[["]]conservative amino acid substitution[["]]" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine),

acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Alternatively, mutations can be introduced randomly along all or part of the coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for their ability to induce anti-IgE antibodies which do not cause anaphylaxis.

<u>Please replace the paragraph beginning on page 20, lines 29-37 and page 21, lines 1-10 as follows:</u>

Expression vectors containing gene inserts can be identified by three general approaches: (a) nucleic acid hybridization; (b) presence or absence of "[["]]marker[["]]" gene functions; and (c) expression of inserted sequences. In the first approach, the presence of antigenic peptide-encoding polynucleotides or antigenic fusion protein-encoding polynucleotides inserted in an expression vector(s) can be detected by nucleic acid hybridization using probes comprising sequences that are homologous to the inserted polynucleotide sequence. In the second approach, the recombinant vector/host system can be identified and selected based upon the presence or absence of certain "[["]]marker[["]]" gene functions (*e.g.*, thymidine kinase activity, resistance to antibiotics, transformation phenotype, occlusion body formation in baculovirus, etc.) caused by the insertion of the gene(s) in the vector(s). For example, if a nucleic acid molecule encoding an antigenic peptide or an antigenic fusion protein is inserted within the marker gene sequence of the vector, recombinants containing the nucleic acid molecule encoding the antigenic peptide or the antigenic fusion protein insert can be identified by the absence of the marker gene function. In the third approach, recombinant expression vectors can be identified by assaying the gene product expressed by the recombinant. Such assays can be based, for example, on the physical or functional properties of an antigenic peptide

or an antigenic fusion protein in *in vitro* assay systems, *e.g.*, binding of an antigenic peptide or an antigenic fusion protein with an anti-IgE antibody.

Please replace the paragraph on page 21, lines 19-23 as follows:

The term "[["]]host cell[["]]" as used herein refers not only to the particular subject cell into which a recombinant DNA molecule is introduced but also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

Please replace the paragraph on page 21, lines 24-35 as follows:

A host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus, expression of the genetically engineered may be controlled. Furthermore, different host cells have characteristic and specific mechanisms for the translational and post-translational processing and modification (*e.g.*, glycosylation, phosphorylation of proteins). Appropriate cell lines or host systems can be chosen to ensure the desired modification and processing of the foreign protein expressed. For example, expression in a bacterial system can be used to produce an unglycosylated core protein product. Expression in yeast will produce a glycosylated product. Expression in mammalian cells can be used to ensure "[["]]native[["]]" glycosylation of an antigenic peptide or antigenic fusion protein of the invention. Furthermore, different vector/host expression systems may effect processing reactions to different extents.

Please replace the paragraph on page 27, lines 1-17 as follows:

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, Calif., U.S.A. (the MaxBat.RTM. kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucle`otide of the present invention is "[["]]transformed.[["]]"

Alternatively, an antigenic peptide of the invention or an antigenic fusion protein of the invention may also be expressed in a form which will facilitate purification. For example, an antigenic peptide may be expressed as fusion protein comprising a heterologous protein such as maltose binding protein (MBP) glutathione-S-transferase (GST) or thioredoxin (TRX) which facilitate purification. Kits for expression and purification of such fusion proteins are commercially available from New England BioLab (Beverly, Mass.), Pharmacia (Piscataway, N.J.) and In Vitrogen, respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("[["]]Flag[["]]") is commercially available from Kodak (New H[[h]]aven, Conn.).

Please replace the paragraph on page 28, lines 1-18 as follows:

An antigenic peptide or an antigenic fusion protein of the invention is "[["]]isolated[["]]" or "[["]]purified[["]]" when it is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "[["]]substantially free of cellular material[["]]" includes preparations of protein in

which the protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, protein that is substantially free of cellular material includes preparations of protein having less than about 30%, 20%, 10%, or 5% (by dry weight) of a contaminating protein. When an antigenic peptide or an antigenic fusion protein of the invention is recombinantly produced, it is also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When an antigenic peptide or an antigenic fusion protein of the invention is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, *i.e.*, it is separated from chemical precursors or other chemicals which are involved in the synthesis of the antigenic peptide or the antigenic fusion protein. Accordingly, such preparations of the protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than the antigenic peptide or the antigenic fusion protein.

Please replace the paragraph beginning on page 30, lines 24-37 and page 31, lines 1-12 as follows:

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of an antigenic peptide or an antigenic fusion protein of the invention, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "[["]]pharmaceutically acceptable[["]]" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "[["]]carrier[["]]" refers to a diluent, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol

solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH[[h]] buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "[["]]Remington''s Pharmaceutical Sciences[["]]" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the antigenic peptide or the antigenic fusion protein, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.